IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Ofer Mandelboim et al.	Confirmation No.: 7654
Application No.: 10/562,735	Patent No.: 7,825,085 B2
Filing Date: May 19, 2006	Patent Date: November 2, 2010
For: FRAGMENTS OF NKP44 AND NKP46 FOR TARGETING VIRAL-INFECTED AND TUMOR CELLS	Attorney Docket No.: 85189-17600

REQUEST FOR CERTIFICATE OF CORRECTION UNDER 37 CFR § 1.322

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

It is requested that a Certificate of Correction be issued in connection with the above-identified patent correcting the errors listed on the accompanying Form PTO-1050. The corrections requested are as follows.

On the Title page, Item (75) Inventors, please correct the spelling of the city of residence of inventor Angel Porgador from "Lehavia" to -- Lehavim --. Support for this change appears on the Application Data Sheet filed with the original application papers on May 19, 2006.

At column 60, line 16 (claim 15, line 3), before "recognition" insert -- the --. Support for this change appears in application claim 47.

This request is being made pursuant to 37 CFR § 1.322 to correct errors that are clerical or typographical in nature and appear to have been made by the Office during the printing of the patent. Therefore, no fee is believed to be due for this request. Should any fees be required, however, please charge such fees to Winston & Strawn LLP Deposit Account No. 50-1814.

Respectfully submitted,

Date: November 5, 2010

Allan A. Fanucci, Reg. No. 30,256

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UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,825,085 B2

APPLICATION NO. : 10/562,735

DATED: : Nov. 2, 2010

INVENTOR(S) : Mandelboim et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Title Page:
Item (75) Inventors, please correct the spelling of the city of residence of inventor Angel Porgador from "Lehavia" to -- Lehavim --.

Column 60:
Line 16 (claim 15, line 3), before "recognition" insert -- the --.

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(12) **United States Patent**
Mandelboim et al.

(10) **Patent No.: US 7,825,085 B2**
(45) **Date of Patent: Nov. 2, 2010**

(54) **FRAGMENTS OF NKP44 AND NKP46 FOR TARGETING VIRAL-INFECTED AND TUMOR CELLS**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 854 days.

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(2), (4) Date: **May 19, 2006**

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(51) **Int. Cl.**

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A61K 38/17	(2006.01)
C07K 14/705	(2006.01)
C07K 9/00	(2006.01)

(52) **U.S. Cl.** **514/8**; 530/322; 530/324; 530/350

(58) **Field of Classification Search** ..... None
See application file for complete search history.

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(57) **ABSTRACT**

The present invention relates generally to peptides derived from the natural cytotoxicity receptors on natural killer (NK) cells and to antibodies against peptide epitopes on these receptors. In particular, the present invention identifies an essential epitope in the proximal domain of NKp46 and NKp44 receptors present on NK cells, as a crucial element for the binding to viral-infected cells. The present invention provides peptides that are derived from the amino acid sequence of NKp46 receptor, capable of specific targeting of viral-infected cells and tumor cells and monoclonal antibodies which recognize a specific domain of NKp46. The present invention further provides hyperglycosylated peptides that are derived from the NKp44 receptor, capable of specific targeting of viral-infected cells.

26 Claims, 12 Drawing Sheets

-continued

Arg Ala Ser Thr Trp Glu Gly Arg Arg Arg Leu Asn Thr Gln Thr Leu
180 185 190

The invention claimed is:

1. An isolated peptide fragment of the natural cytotoxicity receptor NKp46, wherein the peptide fragment comprises a peptide of the D2 domain of the NKp46 receptor that is 20-100 amino acid residues in length and wherein said peptide fragment exhibits at least one activity selected from binding to a viral infected cell or binding to a tumor cell.

2. The peptide fragment of claim **1** comprising at least one glycosylated residue.

3. The isolated peptide fragment of the human NKp46 receptor according to claim **1**, the peptide having the ability to bind to target cells selected from viral-infected cells and tumor cells, with the proviso that said peptide is other than SEQ ID NOs: 1 and 2.

4. The peptide fragment of claim **3** wherein the target cell is of a warm-blooded vertebrate.

5. The peptide fragment of claim **4** wherein the target cell is of human origin.

6. The peptide fragment of claim **3** comprising a minimal epitope of NKp46 receptor having ability to bind to viral-infected cells.

7. The peptide fragment of claim **6** comprising a glycosylated residue corresponding to threonine at position 225 of isoform a of the human NKp46 receptor.

8. The peptide of claim **6** wherein the glycosylated residue comprises sialic acid.

9. The peptide fragment of claim **3** comprising from about 25 to 75 amino acids.

10. The peptide fragment of claim **3** comprising from about 30 to 60 amino acids.

11. A fusion protein comprising an isolated peptide fragment of the natural cytotoxicity receptor NKp46, and further comprising a molecule selected from an immunoglobulin (Ig) molecule or a fragment thereof, and a cytotoxic substance; wherein the peptide fragment comprises a peptide of the D2 domain of the NKp46 receptor that is 20-100 amino acid residues in length; wherein said fusion protein comprising said peptide fragment exhibits at least one activity selected from binding to a viral infected cell or binding to a tumor cell; and wherein said fusion protein is other than the fusion proteins of SEQ ID NOs:13-16.

12. The fusion protein of claim **11** manufactured by recombinant DNA technology or chemical synthesis.

13. The fusion protein of claim **11** comprising the peptide fragment covalently conjugated to a molecule selected from an immunoglobulin (Ig) molecule or a fragment thereof, and a cytotoxic substance.

14. The fusion protein of claim **13** wherein the peptide fragment is covalently conjugated to the Fc fragment of said immunoglobulin molecule.

15. A variant polypeptide of the natural cytotoxicity receptor NKp46, the variant comprising a single amino acid substitution in an epitope required for recognition of viral-infected cells or tumor cells, wherein the epitope is in the proximal domain of the NKp46 receptor a (SEQ ID NO:1), and wherein the single amino acid substitution is at an amino acid residue selected from the group consisting of Threonine 125, Threonine 225 and Asparagine 216.

16. The variant polypeptide of claim **15**, wherein the single amino acid substitution is selected from the group consisting of: Threonine 225 replaced by an amino acid residue selected from the group consisting of Serine, Alanine and Asparagine; Threonine 125 replaced by Alanine, and Asparagine 216 replaced by Alanine.

17. The variant polypeptide of claim **15**, wherein the amino acid substitution is at a glycosylation site within the proximal domain of the NKp46 receptor.

18. The variant polypeptide of claim **15**, comprising at least one glycosylated residue.

19. The variant polypeptide of claim **18**, wherein the glycosylated residue comprises sialic acid.

20. The variant polypeptide of claim **15**, wherein said polypeptide exhibits at least one activity selected from binding to a viral infected cell and binding to a tumor cell.

21. The variant polypeptide of claim **20**, having the ability to bind to viral-infected cells.

22. The variant polypeptide of claim **20**, having the ability to bind to tumor cells.

23. The variant polypeptide of claim **20**, comprising a glycosylated Threonine residue corresponding to Threonine 225 of isoform a of the human NKp46 receptor.

24. The variant polypeptide of claim **23**, wherein the glycosylated residue comprises sialic acid.

25. A fusion protein comprising the variant polypeptide of claim **15**, and further comprising an immunoglobulin (Ig) molecule or a fragment thereof.

26. The fusion protein of claim **25**, comprising the Fc fragment of said immunoglobulin molecule.

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